Efficacy and tolerability of combined treatment with NB-UVB and topical tacrolimus versus NB-UVB alone in patients with vitiligo vulgaris: A randomized intra-individual open comparative trial

Sir,

Narrow-band UVB (NB-UVB) and topical tacrolimus are commonly used treatment options in vitiligo. The primary aim of the study was to assess the additive

effect of tacrolimus ointment in vitiligo patients treated with NB-UVB. The secondary outcome studied was variation in rate of pigmentation according to the body site affected.

The study included 25 consecutive patients (13 males and 12 females, age range 14-36 years) fulfilling the study criteria and consenting for inclusion in the study. Inclusion criteria were generalized vitiligo (5-50% body surface area), stable disease (< 10% change in the last 6 months) and skin types III to VI. Symmetrical vitiligo patches, at least 2 × 2 cm in greatest dimension, on each side of the body served as target lesions. Patients receiving topical or systemic therapy for vitiligo were kept off treatment for 4 weeks prior to start of therapy. Tacrolimus ointment (Topgraf) 0.1% was dispensed to the patients and advised to apply once daily at night on the lesions on one half of the body, which was randomly chosen by a randomization table. The adherence to topical treatment was ensured by asking the patients to return the empty tubes. All patients were treated with NB-UVB in a phototherapy unit (V- care UV therapy unit, Surya 440 ANB). Therapy was administered thrice weekly according to the departmental protocol. The total duration of the study period was 6 months or till complete repigmentation of study lesions if the same occurred earlier. The repigmentation was assessed at week 2, 4, 6, 8, 12, 16, 20 and 24 by serial photographs and area of repigmentation was graded as; absent: 0%; minimal: < 25%; mild: 26-50%; moderate: 51-75%; marked to complete: > 75%. A non-responder of therapy was taken as a patient showing no response or worsening of the disease after 8 weeks of treatment and they were considered as treatment failure.

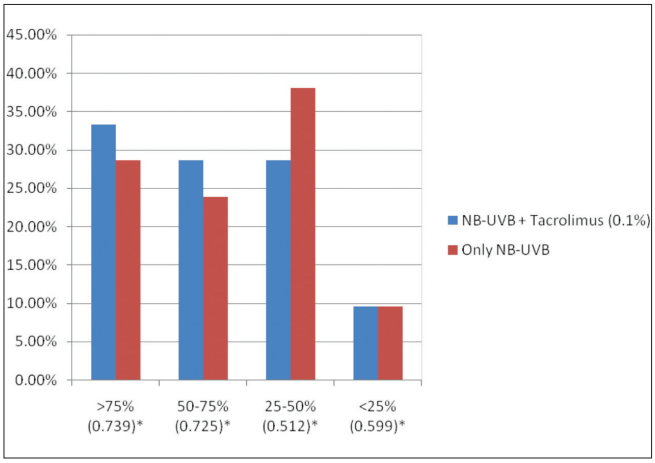

Figure 1: Proportion of patients achieving various grades of pigmentation in NB-UVB + tacrolimus and NB-UVB treated sites (*P value)

Seven (33%) patients in the NB-UVB and tacrolimus combination treated study lesions and 6 (28%) in the NB-UVB treated study lesions had > 75% repigmentation. Though repigmentation was slightly better in the lesions treated with combination of NB-UVB and tacrolimus, the overall difference was not statistically significant [Figure 1]. Grade of repigmentation was strictly dependent on the site; an improvement of more than 50% was obtained more frequently for lesions located on the face and trunk [Table 1]. Four patients were released from treatment in the 6 months study period. Two patients developed new lesions, 1 patient was lost to follow-up and 1 patient did not respond even after 8 weeks of therapy. Twelve patients experienced side effects. There were no adverse effects exclusive to the side on which tacrolimus was applied. No serious adverse reactions were noted and permanent discontinuation due to adverse events never occurred.

Previous reports studying the additive effect of topical tacrolimus and NB-UVB in treatment of vitiligo have shown variable results. In a recent study Nordal *et al*., found combination of NB-UVB and tacrolimus

Table 1: Repigmentation at end of study according to topography

Grade of repigmentation at 24 weeks	Minimal < 25%		Mild (25-50%)		Moderate (50-75%)		Excellent > 75%		Total
Topography	N	T	N	T	N	T	N	T	
Face			2/7 (28)	2/7 (28)	2/7 (28)	1/7 (14)	3/7 (42)	4/7 (57)	7
Trunk			2/4 (50)		1/4 (25)	3/4 (75)	1/4 (25)	1/4 (25)	4
Upper Limb					1/1 (100)	1/1 (100)			1
Lower Limb					1/2 (50)	1/2 (50)	1/2 (50)	1/2 (50)	2
Hands	1/1 (100)	1/1 (100)							1
Feet	1/2 (50)	1/2 (50)	1/2 (50)	1/2 (50)					2
Bony prominence			3/4 (75)	3/4 (75)			1/4 (25)	1/4 (25)	4

*Assessed by serial photographs in a standard position during each visit; N = Narrow band UVB; T = Narrow band UVB + tacrolimus

ointment (0.1%) to be more effective than UV treatment alone in patients with vitiligo.[1] However, NB-UVB was administered for a minimum of 3 months and probably, more patients in the NB-UVB alone arm would have achieved better pigmentation, if phototherapy was given for a longer duration. Other studies with smaller sample size have found better pigmentation in NB-UVB and tacrolimus arm although the difference was not statistically significant.[2,3] In our study 28% of patients had > 75% repigmentation. This is in contrast to the previous studies where higher pigmentation rate was achieved.[4,5] This can be attributed to the fact that in our study 50% of the lesions were at resistant sites, where as in the previous studies the proportions of lesions at resistant sites were less,[4] or such sites were excluded from the analysis.[3,5] Grade of repigmentation was strictly dependent on the site with lesions over face, trunk and limbs showing better outcome. Similar results were obtained in the study by Fai *et al*.[4] The limitations of the study include lack of blinding, use of subjective method in evaluating the extent of repigmentation and small sample size. The lack of statistical significance of difference in repigmentation in our study may be because of the smaller sample size and low power to detect all but large differences, and once daily use of tacrolimus rather than twice daily as currently recommended. Use of tacrolimus is expensive, cumbersome for the patients to apply over large vitiliginous areas and has photo-carcinogenic potential. As the additive effect of topical tacrolimus in combination with NB-UVB has not been fully established, long term prospective studies with larger sample size are required to conclusively establish the role of tacrolimus as an adjunct to NB-UVB in management of vitiligo.

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